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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,530	01/21/2004	Dwight D. Koeberl	5405.280	3856

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EXAMINER	
PATTERSON, CHARLES L JR	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/761,530	KOEBERL ET AL.	
	Examiner	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above claim(s) *19,20 and 30-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 21-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of Group I, claims 1-18 and 21-29 in the reply filed on 7/17/06 is acknowledged. The traversal is on the grounds that there would not be a serious burden upon the examiner toe examine claims 1-72 and in particular groups I-III. Groups I-III are stated to "all recite a chimeric polypeptide comprising a secretory signal sequence operably linked to a lysosomal polypeptide...[and that] the claims of Group I encompasses the same class and subclass as the claims of Group III". This is not found persuasive because, although there is a common class and subclass between Groups I and III, there are several other classes and subclasses in group I and the method of group III is an additional method from the uses of group I, as outlined in the restriction requirement. The reasons for the restriction requirement cited in the requirement are deemed valid and therefore the requirement is maintained. Reconsideration and withdrawal of the restriction requirement between groups I and III will considered after the allowability of Group I is found. However, applicants must comply with all the requirements of MPEP § 821.04.

The requirement is still deemed proper and is therefore made FINAL.

Claims 19-20 and 30-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/17/06.

A review of the priority document (60/441,789) reveals that it only discloses human GAA enzyme with a deletion in the 3' region, corresponding to dependent claims 8-9. It apparently does not disclose the addition of a secretory signal sequence in place of residues 1-27 of SEQ ID NO:2. Therefore, the instant claims are deemed to have priority only to the filing date

of the instant application, 1/21/04, absent a convincing argument to the contrary.

Claims 21 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 21 and 26 are confusing in the recitation of "expressed to produce", which should apparently be "expressing the nucleic acid to produce".

Claim 21 is confusing in the recitation of "and the lysosomal polypeptide secreted from the cell", which should apparently be "and secreting the lysosomal polypeptide from the cell".

Claim 26 is confusing in the recitation of "and the GAA polypeptide secreted from the cultured cell, and collecting the GAA polypeptide secreted into the cell culture medium", which should apparently be "and secreting the chimeric polypeptide from the cultured cell, and collecting the chimeric polypeptide secreted into the cell culture medium".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-18 and 21-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification teaches that the erythropoietin, α-1-antitrypsin and Factor IX leader sequence, when cloned in place of residues 1-27 of SEQ ID NO:2, have increased secretion of hGAA (Table 3). In Table 2, "SP38" is stated to be the source of SEQ ID NO:5 leader sequence while in Table 3 the results are given for "SP38.1". This is not the same thing and therefore it is maintained that there are no results given for the leader sequence of SEQ ID NO:5. Claim 3 recites "prealbumin" as the source of one of the signal sequences, whereas the specification recites "albumin", not "prealbumin" in Table 2 and page 80, line 28. In addition, neither "prealbumin" or "albumin" signal sequence is shown in Table 3 to cause increased secretion.

Claim 9(b) is drawn to a nucleic acid wherein the "3' untranslated region is less than 200 nucleotides in length and comprises a segment that is heterologous to said GAA coding region". The specification does not teach any and all such regions nor can the examiner even find one such embodiment that has been characterized as to the effect of the addition.

It is maintained that the instant claims should be limited to what is taught in the specification, namely erythropoietin, α-1-antitrypsin and Factor IX leader sequences replacing residues 1-27 of SEQ ID NO:2. It is maintained that undue experimentation would be required to practice the invention within the scope of the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 and 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCown, et al.(A). The instant reference teaches that secretory signal peptides may be used to cause secretion of a heterologous protein (abstract). In Example 10 a fibronectin secretory signal sequence is fused to a green fluorescent protein (GFP) in an adeno-associate virus (AAV) and it found that the GFP was secreted into the media whereas the GFP without the secretory signal sequence had GFP throughout the cells. In Example 11 and fibronectin secretory signal sequence fused to the galanin gene in an AAV system produced galanin in the media whereas the galanin gene without the secretory signal sequence did not have galanin secreted in the media. Therefore the reference teaches that if a secretory signal sequence is fused to a protein of interest, the protein will be secreted.

It would have been obvious to one of ordinary skill in the art to fuse a secretory signal sequence to a lysosomal polypeptide with the expectation that the polypeptide would be secreted, as taught by the instant reference. The motivation would have been to secrete the polypeptide into the media where it could be more readily purified. The particular signal sequence used and the identity of the protein to be secreted are deemed to be design choices and would have been obvious absent unexpected results. The pharmaceutical carrier could be water or buffer and also would have been obvious.

Claims 1-18 and 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barash, et al. (4). The instant reference teaches the use of human placental secretory alkaline phosphatase (SEAP) with the natural signal peptide replaced with different secretory signal peptides. They found that the secretory signal peptides caused secretion of the SEAP as they had predicted using a modeling system. The relative strength of the secretion is

shown in Table 2. At least erythropoietin and α-1-antitrypsin present in claim 3 are included in the list.

It would have been obvious to one of ordinary skill in the art to fuse a secretory signal sequence to a lysosomal polypeptide with the expectation that the polypeptide would be secreted, as taught by the instant reference. The motivation would have been to secrete the polypeptide into the media where it could be more readily purified. The particular signal sequence used and the identity of the protein to be secreted are deemed to be design choices and would have been obvious absent unexpected results. The pharmaceutical carrier could be water or buffer and also would have been obvious.

Chen, et al. (U) is cited as of interest in that it teaches the secretion of human α-galactosidase by *Pichia* clones but it does not teach that there is a secretory signal sequence linked to the enzyme gene.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available

through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
September 13, 2006